MAGLUMI Rubella IgM (CLIA)

REF 130212004M

Σ 100

EC REP

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CE 0123

FOR PROFESSIONAL USE ONLY
Store at 2-8 °C

COMPLETELY READ THE INSTRUCTIONS BEFORE PROCEEDING

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SYMBOLS EXPLANATIONS

EC REP	Authorized Representative in the European community
	Manufacturer
	Consult instructions for use
CONT	Contents of kit
IVD	In vitro diagnostic medical device
LOT	Batch code
REF	Catalogue number
	Use by
8°C 2°C	Temperature limitation (store at 2-8 °C)
Σ	Sufficient for
	Keep away from sunlight
	Keep upright for storage.

INTENDED USE

The kit has been designed for the qualitative determination of Rubella IgM in human serum.
The test has to be performed on the Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI (Including Maglumi 600,Maglumi 1000,Maglumi 1000 Plus, Maglumi 2000,Maglumi 2000 Plus,Maglumi 3000 and Maglumi 4000).

SUMMARY AND EXPLANATION OF THE TEST

Rubella is a viral exanthematous infectious disease caused by rubella virus, a single-stranded RNA virus belonging to the Togavirus group. The illness follows a typically benign clinical course with rare complications and is subclinical in a large proportion of cases. Symptomatology is generally mild, characterized by fever, malaise, a maculopapular rash of three to five days' duration and, possibly, coryza and conjunctivitis. The disease is usually accompanied by lymphadenopathy. Infection confers lifelong immunity.
Infection from rubella virus is particularly disastrous if contracted during the first four months of gestation. If not immunologically protected, women infected during pregnancy run a high risk of embryofoetal damage. Congenital rubella causes a wide range of severe defects, many of which are permanent and adversely affect later development (cataract, deafness, hepatosplenomegaly, psychomotor retardation, bone alterations, cardiopathies, and neuropathies). Pathological consequences on the foetus or newborn depend on teratogenicity of the virus and on the time of pregnancy when the infection has been contracted. Gestational age at the time of maternal infection is considered the most important determinant of intrauterine trans- mission and foetal damage. It is generally accepted that the risk decreases with increasing gestational age: it is highest in case of infection during the first two months of pregnancy (40-60%) and progressively decreases during the fourth and fifth months (10-20%). Clinical findings in newborns and virus isolation studies have demonstrated that foetal infection is rare be- yond the second trimester of gestation.
Rubella virus is transmitted in utero during the course of primary maternal infection, whether apparent or inapparent, when the virus in the bloodstream infects the placenta and, subsequently, the foetus. Intrauterine transmission of virus associated with maternal re-infection is extremely rare, indicating that maternal immunity (whether naturally derived or vaccine-induced) protects against intrauterine infection. Maternal infection may result in (a) no infection of the embryo; (b) resorption of the embryo (seen only with infections occurring in the earliest stages of gestation); (c) miscarriage; (d) stillbirth; (e) infection of placenta without foetal involvement or (f) infection of both the placenta and foetus. Infected infants may present obvious multiple organ involvement or, as is frequently observed, no immediately evident disease. However, after long-term follow-up, many of these seemingly unaffected infants have evidence of hearing loss, or central nervous system lesions, or other defects.
The first humoral immune response to infection is the synthesis of specific anti-rubella virus IgM antibody which reaches high serum levels two weeks after the rash and lasts in the circulation for one to two month(s). Specific IgG antibody generally appears a few days after the onset of rash, about one week after IgM develops. It rapidly increases to reach a plateau six to ten weeks after the onset of symptoms and then progressively decreases to a level (15-200 IU/mL) lasting for the whole life. Re-infection, completely asymptomatic, is accompanied by moderately increased levels of specific IgG.
Correct detection of IgM and IgG antibodies to rubella virus

provides an essential tool for diagnosing and following up acute infection, for assessment of immune status in fertile women, and therefore for adopting suitable prophylaxis in susceptible women of child-bearing age. Since when a vaccine was made available, the assay of IgG to rubella virus has been widely used to determine seroconversion of the recipient after vaccination.

PRINCIPLE OF THE TEST

Indirect immunoluminometric assay:

Mouse anti-human IgM is used to label ABEI, and use purified Rubella antigen to coat nano magnetic microbeads. Sample, Calibrator or Control with Buffer （goat Anti-human IgG goat Anti-human IgA） and nano magnetic microbeads coated with Rubella antigen are mixed thoroughly and incubated at 37℃ and cycle washing for 1 time. Then add ABEI Label, incubation and form a sandwich, then washing for the 2nd time. Subsequently, the starter reagents are added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as RLU within 3 seconds and is proportional to the concentration of Rubella IgM present in samples.

CONT KIT COMPONENTS

Material Supplies

Reagent Integral for 100 determinations	
Nano magnetic microbeads: TRIS buffer, 1.2% (W/V), 0.2%NaN_3, coated with Rubella antigen	2.5ml
Calibrator Low: bovine serum, 0.2%NaN_3.	2.5ml
Calibrator High: bovine serum, 0.2%NaN_3	2.5ml
Buffer: Goat anti-Human IgA 1.2%(W/V), Goat anti-Human IgG, 0.2%NaN_3, BSA	22.5ml
ABEI Label: Mouse anti-human IgM labeled ABEI contains BSA, 0.2%NaN_3.	22.5ml
All reagents are provided ready-to-use.	

Reagent Vials in kit box	
Internal Quality Control: containing BSA, 0.2%NaN_3. (target value refer to Quality Control Information date sheet)	2.0ml

Internal quality control is only applicable with MAGLUMI system. Instructions for use and target value refer to Quality Control Information date sheet. User needs to judge results with their own standards and knowledge.

Accessories Required But Not Provided

MAGLUMI Reaction Module	REF: 630003
MAGLUMI Starter 1+2	REF: 130299004M
MAGLUMI Wash Concentrate	REF: 130299005M
MAGLUMI Light Check	REF: 130299006M

Please order accessories from SNIBE or our representative.

Preparation of the Reagent Integral

Before the sealing is removed, gentle and careful horizontal shaking of the Reagent Integral is essential (avoid foam formation!) Remove the sealing and turn the small wheel of the magnetic microbeads compartment to and fro, until the colour of the suspension has changed into brown. Place the Integral into the reagent area and let it stand there for 30 min. During this time, the magnetic microbeads are automatically agitated and completely resuspended.

Do not interchange integral component from different reagents or lots!

Storage and Stability

- Sealed: Stored at 2-8℃ until the expiry date.
- Opened: Stable for 4 weeks. To ensure the best kit performance, it is recommended to place opened kits in the refrigerator if it's not going to be used on board during the next 12 hours.
-  Keep upright for storage.
-  Keep away from sunlight.

CALIBRATION AND TRACEABILITY

1) Traceability

To perform an accurate calibration, we have provided the test calibrators standardized against the SNIBE internal reference substance.

Calibrators in the Reagent Kit are from Fitzgerald.

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2) 2-Point Recalibration

Via the measurement of calibrators, the predefined master curve is adjusted (recalibrated) to a new, instrument-specific measurement level with each calibration.

3) Frequency of Recalibration

- After each exchange of lots (Reagent Integral or Starter Reagents).
- Every week and/or each time a new Integral is used (recommendation).
- After each servicing of the Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI.
- If controls are beyond the expected range.
- The room temperature has changed more than 5 ℃ (recommendation).

SPECIMEN COLLECTION AND PREPARATION

Sample material: serum

Collect 5.0ml venous blood into Blood Collection Tube (Tube without anticoagulant or coagulant, Anticoagulation tube with EDTA-K_2 or EDTA-Na_4 can be used. Anticoagulation tube with heparin sodium is not recommended).

Standing at room temperature，centrifuging, separating serum part. The serum sample is stable for up to 12 hours at 2-8℃. If preserved for more than 12 hours, please packed, -20 ℃ can be stored for 30 days.

Avoid repeated freezing and thawing, the serum sample can be only frozen and thawed two times. Stored samples should be thoroughly mixed prior to use (Vortex mixer).

Please ask local representative of SNIBE for more details if you have any doubt.

Vacuum Tubes

(a) Blank tubes are recommended type for collecting samples.

(b) Please ask SNIBE for advice if special additive must be used in sample collecting.

Specimen Conditions

- Do not use specimens with the following conditions:
  (a) heat-inactivated specimens;
  (b) Cadaver specimens or body fluids other than human serum;
  (c) Obvious microbial contamination.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- Inspect all samples for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each sample to prevent cross contamination.
- Serum specimens should be free of fibrin, red blood cells or

other particulate matter.

- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time. If the specimen is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results.

Preparation for Analysis

- Patient specimens with a cloudy or turbid appearance must be centrifuged prior to testing. Following centrifugation, avoid the lipid layer (if present) when pipetting the specimen into a sample cup or secondary tube.
- Specimens must be mixed **thoroughly** after thawing by **low** speed vortexing or by gently inverting, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results. Multiple freeze-thaw cycles of specimens should be avoided.
- All samples (patient specimens or controls) should be tested within 3 hours of being placed on board the MAGLUMI System. Refer to the SNIBE service for a more detailed discussion of onboard sample storage constraints.

Storage

- If testing will be delayed for more than 8 hours, remove serum from the serum separator, red blood cells or clot. Specimens removed from the separator gel, cells or clot may be stored up to 12 hours at 2-8°C.
- Specimens can be stored up to 30 days frozen at -20°C or colder.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the serum separator, red blood cells or clot. When shipped, specimens must be packaged and labeled in compliance with applicable state, federal and international regulations covering the transport of clinical specimens and infectious substances. Specimens must be shipped frozen (dry ice). Do not exceed the storage time limitations identified in this section of the package insert.

WARNING AND PRECAUTIONS FOR USERS

IVD

- For use in *IN-VITRO* diagnostic procedures only.
- Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

CAUTION: This product requires the handling of human specimens.

- The calibrators in this kit are prepared from bovine serum products. However, because no test method can offer complete assurance that HIV, Hepatitis B Virus or other infectious agents are absent; these reagents should be considered a potential biohazard and handled with the same precautions as applied to any serum or plasma specimen.
- All samples, biological reagents and materials used in the assay must be considered potentially able to transmit infectious agents. They should therefore be disposed of in accordance with the prevailing regulations and guidelines of the agencies holding jurisdiction over the laboratory, and the regulations of each country. Disposable materials must be incinerated; liquid waste must be decontaminated with sodium hypochlorite at a final concentration of 5% for at least half an hour. Any materials to be reused must be autoclaved using an overkill approach. A minimum of one hour at 121℃ is usually considered adequate, though the users must check the effectiveness of their decontamination cycle by initially validating it and routinely using biological indicators.
- It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens13. Biosafety Level 214 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.
- This product contains Sodium Azide; this material and its container must be disposed of in a safe way.
- Safety data sheets are available on request.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- Do not mix reagents from different reagent kits.
- Prior to loading the Reagent Kit on the system for the first time, the microbeads requires mixing to re-suspend microbeads that have settled during shipment.
- For microbeads mixing instructions, refer to the KIT COMPONENTS, Preparation of the Reagent Integral section of this package insert.
- To avoid contamination, wear clean gloves when operating with a reagent kit and sample.
- Over time, residual liquids may dry on the kit surface, please pay attention the silicon film still exists on the surface of the kit.
- For a detailed discussion of handling precautions during system operation, refer to the SNIBE service information.

TEST PROCEDURE

To ensure proper test performance, strictly adhere to the operating instructions of the Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI. Each test parameter is identified via a RFID tag on the Reagent Integral. For further information please refer to the Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI. Operating Instructions.

10μl +200μl	Sample, calibrator Buffer
10 min	Incubation
+20μl	Nano magnetic microbeads
10 min	Incubation
400μl	Cycle washing
+200μl	ABEI Label
10 min	Incubation
400μl	Cycle washing
3 s	Measurement

* Do not interchange magnetic microbeads from different lots.

QUALITY CONTROL

- Observe quality control guidelines for medical laboratories
- Use suitable controls for in-house quality control. Controls should be run at least once every 24 hours when the test is in use, once per reagent kit and after every calibration. The control intervals should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined ranges. Each laboratory should establish guidelines for corrective measures to be taken if values fall outside the range.

LIMITATIONS OF THE PROCEDURE

1) Limitations

Use Rubella IgM value as a kind of auxiliary material for other testing data when in diagnosis. Assay results should be utilized in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions

A skillful technique and strict adherence to the instructions are

necessary to obtain reliable results. Bacterial contamination of samples or repeated freeze-thaw cycles may affect the test results. Assay results should be utilized in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions.

2) Interfering Substances

No interference with test results is seen by concentrations of bilirubin ≤ 0.4mg/ml, haemoglobin ≤ 10mg/ml， Triglycerides ≤ 20mg/ml.

3) HAMA

Patient samples containing human anti-mouse antibodies (HAMA) may give falsely elevated or decreased values. Although HAMA-neutralizing agents are added, extremely high HAMA serum concentrations may occasionally influence results.

RESULTS

1) Calculation of Results

- The analyzer automatically calculates the Rubella IgM concentration in each sample by means of a calibration curve which is generated by a 2-point calibration master curve procedure. The results are expressed in AU/ml. For further information please refer to the Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI Operating Instructions.

2) Interpretation of Results

Results obtained with the MAGLUMI Rubella IgM assay can be interpreted as follows:

- Non-reactive: A result less than 2 AU/ml (< 2 AU/ml) is considered to be negative.
- Reactive: A result greater than or equal to 2 AU/ml is (≥ 2 AU/ml) considered to be positive.

Since there is no Rubella IgM international standard material yet, different IVD manufacturer have different traceability chain. Therefore results from assays of other manufacturers cannot be used interchangeably.

PERFORMANCE CHARACTERISTICS

1) Precision

Intra-assay coefficient of variation was evaluated on 3 different levels of control serum repeatedly measured 20 times in the same run, calculating the coefficient of variation.

Intra-assay precision			
Control	Mean(AU/ml)	SD(AU/ml)	CV%
Level 1	1.49	0.08	5.65
Level 2	6.55	0.36	5.44
Level 3	19.81	0.94	4.75

Inter-assay coefficient of variation was evaluated on three batches of kits. Repeatedly measured 3 different levels of control serum 21 times, calculating the coefficient of variation.

Inter-assay precision			
Control	Mean(AU/ml)	SD(AU/ml)	CV%
Level 1	1.55	0.14	8.86
Level 2	6.61	0.58	8.75
Level 3	19.51	1.68	8.61

2) Analytical Sensitivity

The sensitivity is defined as the concentration of Rubella IgM equivalent to the mean RLU of 20 replicates of the zero standard plus two standard deviations corresponding to the concentration from the standard curve. The sensitivity is typically less than 0.25 AU/ml.

3) Specificity

The specificity of the Rubella IgM assay system was assessed by measuring the apparent response of the assay to various potentially cross reactive analytes.

When CMV IgG, CMV IgM, Rubella IgG, Toxo IgG, Toxo IgM, HSV-1/2IgG, HSV-1/2IgM separately reach a concentration of 30AU/ml, measured Rubella IgM is negative. No cross reaction with the IgG or IgM antibody of HAV, HBV, HCV, HIV, syphilis, EBV. The ELISA diagnosed RF or ANA positive, which is non Rubella infected sample, this reagent's determination results show negative.

4) Recovery

Consider calibrator high of known concentration as a sample, dilute it by 1:2 ratio with diluents, and measure its diluted concentration for 10 times. Then calculate the recovery of measured concentration and expected concentration. The recovery should be within 90% -110%.

Expected	Mean Measuring	Recovery
9.8 AU/ml	9.6AU/ml	98%

REFERENCES

1. Best, J. M., S. O'Shea, G. Tipples, N. Davies, S. M. Al Khusaiby, A. Krause, L. M. Hesketh, L. Jin, and G. Enders. 2002. Interpretation of rubella serology in pregnancy—pitfalls and problems. BMJ 325:147-148.
2. Dwyer, D. E., P. W. Robertson, and P. R. Fields. 2001. Broadsheet: clinical and laboratory features of rubella. Pathology 33:322-328.
3. Field, P. R., V. Sintchenko, and G. L. Gilbert. 1998. Confirmation of rubella infection: review of 10 years' experience at ICPMR. Inoculum 7:1-3.
4. Francis, B. H., A. K. Thomas, and C. A. McCarty. 2003. The impact of rubella immunization on the serological status of women of childbearing age: a retrospective longitudinal study in Melbourne, Australia. Am. J. Public Health 93:1274-1276
5. Gutiérrez, A., M. J. Rodríguez, F. De Ory, G. Piédrola, and M. C. Maroto. 1999. Reliability of low-avidity IgG and of IgA in the diagnosis of primary infection by rubella virus with an adaptation of a commercial test. J. Clin. Lab. Anal. 13:1-4.